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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/616,410	07/08/2003	Tony Hunter	066671-0043	9290

54244 7590 08/26/2005

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EXAMINER

YAO, LEI

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 08/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/616,410

Applicant(s)

HUNTER ET AL.

Examiner

Lei Yao, Ph.D.

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 8-25-2003.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 4-30 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 4-30 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: Exhibit A, B

DETAILED ACTION

The office action is written in the reply filed on 08/25/2003.

Claims 1-4 have been cancelled. Claims 4-30 have been added. Claims 4-30 are pending and are examined on the merits.

Specification Objections

The specification is objected to for lacking cross-reference information to parent applications.

Priority

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

Applicant's claims to an earlier effective filing date through an US application 09/275900 ('900), filed on 03/24/1999, is acknowledged. Applicant's claims to an earlier effective filing date through an US application 08/555912 ('912), filed on 11/13/1995, is acknowledged. Claims 4-30 are drawn to a nucleic acid comprising nucleotides 13-129 or 175-489 of SEQ ID NO: 1 and a nucleic acid encoding a portion of Pin1 polypeptide comprising an amino acid 5-43 or 59-163 of SEQ ID NO: 2, which substantially have protein-protein interaction activity or PPlase activity. Upon review of specification of the applications, it is noted that then neither '900 nor '912 of applications provide adequate written description of the genus of nucleotides comprising nucleotides 13-129 or 175-489 of SEQ ID NO: 1 or nucleic acid encoding a genus of polypeptides comprising an amino acid 5-43 or 59-163 of SEQ ID NO: 2. Therefore, Claims 4-30 will be given priority to the instant filing date of July 8, 2003.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the **second paragraph** of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 4-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4-30 are indefinite for the recitation of " nucleotide sequence substantially the same as nucleotide 13-129 or 175-489 of SEQ ID NO: 1" or "a nucleotide sequence or a nucleotide sequence variant encoding a portion of a Pin1 polypeptide having substantially the same sequence as amino acid 5-43 or 59-163 of SEQ ID NO: 2". It is unclear how much structural difference from nucleotides 13-129, 175-489, and amino acids 5-43 and 59-163 is tolerated within the metes and bounds of "substantially the same".

Claims 4 and 18 are vague and indefinite in the recitation of "at least about 15 contiguous nucleotides". It is unclear how much variation from 15 nucleotides is permitted by the term "about".

2. The following is a quotation of the **first paragraph** of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

As drawn to new matter

Claims 4-30 have been amended to recite nucleic acid residues 13-129 and 175-489 of SEQ ID NO: 1 or a nucleotide comprising a degenerate nucleotide sequence variant encoding a portion of a Pin1 polypeptide having substantially the same amino acid sequence as amino acid 5-43 and 59-163 of SEQ ID NO: 2. The specification as filed, although identifying the regions of the Pin1 protein comprising the WW domain at residues 5-43 and the PPlase domain at residues 59-163 of SEQ ID NO: 2, does not provide sufficient support for the instant amendment claims reciting nucleic acid residues which minimally comprise 13-129 or 175-489 of SEQ ID NO: 1 or nucleotide comprising nucleotide sequence encoding a Pin1 polypeptide minimally comprising substantially the same amino acid sequence as amino acid 5-43 and 59-163 of SEQ ID NO: 2 because the term "substantially the same" allows for a variation in sequence from amino acids 5-43 and 59-163 and because the claims encompass sequences which vary considerably from SEQ ID NO:1 or the polynucleotides which encode SEQ ID NO:2.

As drawn to written description

Claims 4-5 and 18-19 are drawn to an isolated nucleic acid comprising a nucleotide sequence **substantially the same** as nucleotide or hybridize to 13-129 or 175-489 of SEQ ID NO: 1. Claims 6-17 dependent on claim 4, which comprise a nucleotide sequence or **sequence variant** encoding a **portion of Pin1** polypeptide having **substantially the same** amino acid sequence, which exhibits the same protein-protein interaction activity and NIMA mitotic kinase binding activity as amino acid 5-43 of SEQ ID NO: 2. Claims 20-30 dependent on claim 18, which comprise a nucleotide sequence or sequence variant encoding a portion of Pin1 polypeptide having substantially the same amino acid sequence, which exhibit the same PPlase activity as amino acids 59-163 of SEQ ID NO: 2.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

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The claims recite sequence substantially the same as nucleotide or hybridize to 13-129 or 175-489 of SEQ ID NO: 1 or sequence variant encoding a portion of Pin1 polypeptide having substantially the same amino acid sequence as amino acid 5-43 or 59-163 of SEQ ID NO: 2, which exhibit the same protein-protein interaction activity, NIMA mitotic kinase binding activity or PPlase activity. The claims do not limit any particular conserved structural attributes because no metes or bounds can be determined for the terms "substantially the same", "sequence variant" or "a portion of Pin1 polypeptide". The specification merely discloses nucleotide of SEQ ID NO: 1 and Pin1 polypeptide of SEQ ID NO: 2, which has a protein-protein activity and PPlase activity. No sequence variant and substantially the same as nucleotide of 3-129 or 175-489 of SEQ ID NO: 1 and no any portion of the Pin1 polypeptide and substantially the same as amino acid sequence of 5-43 or 59-163 of SEQ ID NO: 2 meeting the limitation of the claims were ever identified or particular described. No NIMA mitotic kinase binding activity or PPlase activity exhibited by a portion of the Pin1 polypeptide or a polypeptide substantially the same as amino acid sequence of 5-43 or 59-163 of SEQ ID NO: 2 were described. Therefore, the instant claims encompass signification structural dissimilarity as compared to the SEQ ID NO: 1 or Pin1 polypeptide or polypeptide of SEQ ID NO: 2. The SEQ ID NO: 1, Pin 1 polypeptide, or SEQ ID NO: 2 does not anticipate the claimed genus because the genus includes molecules which differ widely both in functional attributes and structural attributes from SEQ ID NO: 1, or nucleotide encoding Pin 1 or SEQ ID NO: 2.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is partial structures in the form of a recitation of a nucleotide sequence substantially the same as nucleotide 13-129 or 175-489 of SEQ ID NO: 1, or a nucleotide sequence variant or a sequence encoding a portion of polypeptide of 5-43 or 59-163 of SEQ ID NO: 2. There is no identification of any particular portion of the structure that must be conserved except nucleotide 13-129 or 175-489 of SEQ ID NO: 1, or a nucleotide sequence encoding a portion of polypeptide of 5-43 or 59-163 of SEQ ID NO: 2. The instant specification does not set forth that

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particular sequence variant encoding any particular portion of the amino acid sequence of SEQ ID NO: 2 has protein-protein interaction or PPlase activity except a nucleotide sequence encoding a polypeptide of 5-43 or 59-163 of SEQ ID NO: 2.

Protein chemistry is probably one of the most unpredictable areas of biotechnology. It is well known in the art that proteins are folded 3-dimensional structures, the function and stability of which are directly related to a specific conformation (Mathews and Van Holde, Biochemistry, 1996, pp. 165-171). In any given protein, amino acids distant from one another in the primary sequence may be closely located in the folded, 3-dimensional structure (Mathews and Van Holde, Biochemistry, 1996, pp. 166, figure 6.1). It is also known in the art that even a single modification or substitution in a protein sequence can alter the protein function including ability of protein-protein interaction. For example, the replacement of a single lysine at position 118 of the acidic fibroblast growth factor by aglutamic acid led to a substantial loss of heparin binding, receptor binding, and biological activity of the protein (Burgess et al, Journal of Cell biology, Vol 111, p2129-2138, 1990).

The instant specification does not provide a specific functional characteristic of a nucleotide sequence substantially the same as nucleotide 13-129 or 175-489 of SEQ ID NO: 1. The instant specification does not provide a specific functional characteristics of the nucleotide sequence or nucleotide sequence variant encoding a portion of polypeptide having substantially the same sequence as amino acid 5-43 or 59-163 of SEQ ID NO: 2. Accordingly, in the absence of sufficient recitation of distinguishing structural and functional characteristics, the specification does not provide adequate written description of the claimed genus. Therefore, the written description is not commensurate in scope with the claims, which read on a nucleotide sequence substantially the same as nucleotide 13-129 or 175-489 of SEQ ID NO: 1 or nucleotide sequence variant encoding a portion of polypeptide having substantially the same sequence as amino acid 5-43 or 59-163 of SEQ ID NO: 2. One of skill in the art would reasonably conclude that applicant was not in possession of the claimed genus.

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*,

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25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. Therefore, only isolated nucleic acid consisting nucleotide sequence 13-129 or 175-489 of SEQ ID NO: 1 and isolated nucleic acid encoding an amino acid 5-43 or 59-163 of SEQ ID NO: 2, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

1. The compliment of claim 4 in part is rejected under 35 U.S.C. 102(b) based upon a public use or sale of the invention (#1230, Random Primer, New England Biolabs, Catalog 1993/4).

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The catalog of New England Biolabs discloses a random primer (Catalog# 1230), which is a complement of the claimed isolated nucleic acid. It is noted that claim 4 as written does not require that the complement is limited to having at least 15 nucleotides.

2. Claims 4-30 are rejected under U.S.C. 102(e) as being anticipated by Baker et al., (Publication of US patent application 2003/0225528 A1).

Baker et al., disclose a nucleotide sequence (SEQ ID NO: 338, Pin1), comprising a sequence, which is 100% identical to the sequence of 13-129 and 175-489 of SEQ ID NO: 1 as evidenced by sequence search (see attachment, Exhibit B). Baker et al., further disclose that Pin1 is proliferation makers in cell growth, which has a mitotic activity (Section 426).

3. Claims 18-30 are rejected under 35 U.S.C. 102(e) as being anticipated by Mattews et al., (Publication of US patent application 2004/0171019 A1).

Mattews et al., disclose a nucleic acid sequence, residue 64-423 of SEQ ID NO: 1, which is 100% identical to the nucleotide residue 157-516 of SEQ ID NO: 1 as evidenced by sequence search (see attachment, Exhibit A). Mattews et al., further disclose that nucleic acid sequence encodes a polypeptide, which contains Pin1 PPlase domain (Section 0025).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lei Yao, Ph.D. whose telephone number is 571-272-3112. The examiner can normally be reached on 8am-4.30pm Monday to Friday.

Any inquiry of a general nature, matching or file papers or relating to the status of this application or proceeding should be directed to Kim Downing for Art Unit 1642 whose telephone number is 571-272-0521

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lei Yao, Ph.D.
Examiner
Art Unit 1642

LY


KAREN A. CANELLA PH.D
PRIMARY EXAMINER

XX	AAZ33510	standard; cDNA; 580 BP.
XX	ID	AAZ33510 standard; cDNA; 580 BP.
XX	AC	AAZ33510;
XX	DT	08-DEC-1999 (first entry)
XX	DE	Human prostate cancer-associated EST 34.
XX	KM	Expressed sequence tag; EST; prostate; tumor; treatment; gene therapy;
XX	KW	cancer; tissue specificity; human; ss.
OS	Homo sapiens.	
PN	DE19811194-A1.	
PD	16-SEP-1999.	
PF	10-MAR-1998; 98DE-01011194.	
PR	10-MAR-1998; 98DE-01011194.	
XX	(META-) METAGEN GES GENOMFORSCHUNG MBH.	
PA	Specht T, Hinzmann B, Schmitt A, Pilarsky C, Dahl E, Rosenthal A;	
PI	WPI: 1999-519629/44.	
DR	P-PSDB; MAY48377.	
PT	New nucleic acid expressed at high level in normal prostatic tissue and	
PT	encoded polypeptides, used to treat cancer and screen for therapeutic	
PT	agents.	
PS	Claim 3; 101; 194pp; German.	
CC	This invention describes novel nucleic acid sequences (A) that are	
CC	expressed at high level in normal prostatic tissue. Polypeptides (1)	
CC	encoded by (A) are used: (a) for identifying agents for treatment of	
CC	prostatic cancer and (b) for therapy of prostate cancer, optionally where	
CC	expressed by gene therapy methods. (A) is also used to isolate full-	
CC	length genes (for gene therapy) and for recombinant production of (1),	
CC	which can be used to raise specific antibodies. (A) are identified by	
CC	assembly of ESTs (expressed sequence tags) before these are analyzed for	
CC	expression pattern (tissue specificity). This approach eliminates many of	
CC	the false results, as regards tissue specificity, associated with known	
CC	methods that use single (usually short) ESTs. AA23477-23540 represent	
CC	expressed sequence tags described in the method of the invention	
SQ	Sequence 580 BP; 124 A; 163 C; 213 G; 80 T; 0 U; 0 Other;	
Query Match	41.9%; Score 425; DB 2; Length 580;	
Beet Local Similarity	100.0%; Pred. No. 5.6e-146; Indels 0; Gaps 0;	
Matches	425; Conservative 0; Mismatches 0;	
Dy	17 GAGGGAAGATGGCGGACGAGAGAAGCTGCCGCCGCTGGGAGAAGCGCATGACC CGCA	76
Db	36 GAGGGAAGATGGCGGACGAGAGAAGCTGCCGCCGCTGGGAGAAGCGCATGACC CGCA	95
Dy	77 GCTCAGGCCGAGGTGTAATTCAACAACATCACTTAAAGCCAGCGAGTGAGGCGGCCCA	136
Db	96 GCTCAGGCCGAGGTGTAATTCAACAACATCACTTAAAGCCAGCGAGTGAGGCGGCCCA	155
Dy	137 GGCGGAAGAGAGAGCTGTGGCAA AAAACGGGCAGAGGGGAGCTGCCAGGCTCCGCTCT	196
Db	156 GGCGGAAGAGAGAGCTGTGGCAA AAAACGGGCAGAGGGGAGCTGCCAGGCTCCGCTCT	215
Dy	197 CGCACCTGCTGTGAAGACAGCCAGTCAGCGCGGCGCTCTGCTCTGCGCGGAGAGAGA	256
Db	216 CGCACCTGCTGTGAAGACAGCCAGTCAGCGCGGCGCTCTGCTCTGCGCGGAGAGAGA	275
Dy	257 TCACCAGGACCAAGAGAGGCGCTGAGCTGATCAACGACTTAACTCCAGAGATCAAGT	316

Db 276 TCACCCGCAACAAGAGAAGGCCCTCGAGCTGTATCAAGGGTACTCATTCAGAAAGTCAAGT 335
QY 317 CGGAGAGAGAGAGACTTTGAGTCTCTGSGCTCAAGTTCAGAGACTGCAGCTCAGCCAAG 378
Db 336 CGGAGAGAGAGAGACTTTGAGTCTCTGSGCTCAAGTTCAGAGACTGCAGCTCAGCCAAG 399
QY 377 CCAAGGAGAGACTGGGTGCTTCACAGAGAGTGAGTCAAGAACCAATTGAAGACGCT 438
Db 396 CCAAGGAGAGACTGGGTGCTTCACAGAGAGTGAGTCAAGAACCAATTGAAGACGCT 455

QY 437 CGTTT 441
|||
Db 456 CGTTT 460

RESULT 10
AD128801.
ID AD128801 standard; cDNA, 423 BP.
XX AC
XX AD128801;
XX DT 22-APR-2004 (first entry)
XX XX
DE Human PIN1 peptidyl-prolyl isomerase domain coding sequence.
XX Human; PIN1; peptidyl-prolyl isomerase; enzyme; gene; ss.
OS Homo sapiens.
XX
XX
XX Key Location/Qualifiers
FH 1..423
FT CDS /*tag= a
FT 62..420
FT mat_peptide /*tag= b
FT /product= "PIN1 PIase domain"
PN
XX MO2004005315-A2.
XX PD 15-JAN-2004.
PF 27-JUN-2003; 2003WO-IB003101.
PR 09-JUL-2002; 2002US-0394889P.
PS (PIFZ) PFIZER INC.
PI Matthews DA, Dagostino EF, Ferre RA, Gaur S, Guo C, Hou X,
PI Margosiak S, Mroczkowski B, Nakayama GR, Parge HE, Zhu YJ;
XX MPI: 2004-099367/10.
XX R-PSDB; AD128802.
DR Novel poly(amide) containing PIN1 peptidyl-prolyl isomerase domain useful
XX for drug discovery and for designing for the identification and design of
XX modulators of PIN1 peptidyl-prolyl isomerase activity.

Claim 2: SEQ ID NO 1; 63pp: English.

The present sequence is the coding sequence of the peptidyl-prolyl
isomerase (PIase) domain of human PIN1, as expressed from plasmid pET-
28a which contains a 6His tag and a thrombin cleavage site. PIN1 is a
phosphorylation-dependent PIase and a regulator of Cd25. The invention
relates to mutant PIN1 polypeptides containing the PIase domain but not
containing the PIN1 WW domain, and to the polynucleotides that encode
them. It also relates to the X-ray crystal structures of these
polypeptides and to the X-ray crystal structures of the mutant PIN1
PIase polypeptides and small entities that bind to the PIN1 PIase
substrate-binding domain. The structure coordinate data derived from
these crystals provides a three-dimensional description of the substrate-
binding site of PIN1 PIase useful in drug discovery and design for the
identification and design of modulators of PIN1 PIase activity.

Sequence 423 BP; 93 A; 124 C; 140 G; 66 T; 0 U; 0 Other;

Exhibit B

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Db 61 AAGCGCATGAGCCGCGAGCTCAGGCGGAGTACTACTCAACCATCATCACTAAGCCAGC 120
Qy 121 CAGTGGGAGGGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGG 180
Db 121 CAGTGGGAGGGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGG 180
Qy 181 GCGAGGGTCCGCTGCTGCGACCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTG 240
Db 181 GCGAGGGTCCGCTGCTGCGACCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTG 240
Qy 241 TGGCGGCGGAGAGATCACTCCGCGACCAAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 300
Db 241 TGGCGGCGGAGAGATCACTCCGCGACCAAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 300
Qy 301 ATCCAGAGATCACTCCGCGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 360
Db 301 ATCCAGAGATCACTCCGCGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 360
Qy 361 TGCAGCTCAGCCAGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGG 420
Db 361 TGCAGCTCAGCCAGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGG 420
Qy 421 CCATTGGAAGAGCTCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTG 480
Db 421 CCATTGGAAGAGCTCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTG 480
Qy 481 GATTCCGCGCATCACTCATCTCTGCGCATGAGTGAAGGAGGAGGAGGAGGAGGAGGAGGAGG 540
Db 481 GATTCCGCGCATCACTCATCTCTGCGCATGAGTGAAGGAGGAGGAGGAGGAGGAGGAGGAGG 540
Qy 541 CGGCGGAGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGG 600
Db 541 CGGCGGAGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGG 600
Qy 601 ACCCGCGCATCTCCGCGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCG 660
Db 601 ACCCGCGCATCTCCGCGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCG 660
Qy 661 GCCCTTCAGAGTGGGGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGG 720
Db 661 GCCCTTCAGAGTGGGGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGG 720
Qy 721 GACCGCGCATCTCTCTTAAGAAATGACTTCAAGAGGAGGAGGAGGAGGAGGAGGAGGAGGAG 780
Db 721 GACCGCGCATCTCTCTTAAGAAATGACTTCAAGAGGAGGAGGAGGAGGAGGAGGAGGAGGAG 780
Qy 781 GGGCGAGTGGTGGGAGGAGGAGGAGGAGGAGGAGGAGGAGGAGGAGGAGGAGGAGGAGGAGG 840
Db 781 GGGCGAGTGGTGGGAGGAGGAGGAGGAGGAGGAGGAGGAGGAGGAGGAGGAGGAGGAGGAGG 840
Qy 841 TCCCGCGAGTGGTGGGAGGAGGAGGAGGAGGAGGAGGAGGAGGAGGAGGAGGAGGAGGAGGAG 900
Db 841 TCCCGCGAGTGGTGGGAGGAGGAGGAGGAGGAGGAGGAGGAGGAGGAGGAGGAGGAGGAGGAG 900
Qy 901 TCTGTTCAAGTGGCAAAAGTGAACTCATGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGG 960
Db 901 TCTGTTCAAGTGGCAAAAGTGAACTCATGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGG 960
Qy 961 CAGACCCCTTCACCCCCAATTAAACCAAGAACCACTAATAAAAAAAAAAAAAAAAAAAAA 1014
Db 961 CAGACCCCTTCACCCCCAATTAAACCAAGAACCACTAATAAAAAAAAAAAAAAAAAAAAA 1014

```

RESULT 5
 US-10-388-360-338
 Sequence 338, Application US/10388360
 Public Information No. US20030225528A1
 GENERAL INFORMATION:
 APPLICANT: GENOMIC HEALTH
 APPLICANT: Baker, Joffe B.
 APPLICANT: Cronin, Maureen T.
 APPLICANT: Kiefer, Michael C.
 APPLICANT: Shah, Steve

Exhibit B

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APPLICANT: Walker, Michael Graham
TITLE OF INVENTION: GENE EXPRESSION PROFILING IN BIOPSYED TUMOR TISSUES
FILE REFERENCE: 39740-0001US
CURRENT APPLICATION NUMBER: US/10/388,360
CURRENT FILING DATE: 2003-03-12
PRIOR APPLICATION NUMBER: US 60/412,049
PRIOR FILING DATE: 2002-09-18
PRIOR APPLICATION NUMBER: US 09/364,890
PRIOR FILING DATE: 2002-03-13
NUMBER OF SEQ ID NOS: 384
SOFTWARE: FastSeq for NINDS Version 4.0
SEQ ID NO 338
LENGTH: 994
TYPE: DNA
ORGANISM: Homo sapiens
US-10-388-360-338

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Query Match 98.0%; Score 994; DB 17; Length 994;
 Best Local Similarity 100.0%; Pred. No. 6,4e-269; Indels 0; Gaps 0;
 Matches 994; Conservative 0; Mismatches 0;

```

Qy 1 TGCCTGCGCAGACCTCGAGGAGAGATGCGGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 60
Db 1 TGCCTGCGCAGACCTCGAGGAGAGATGCGGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 60
Qy 61 AAGCGCATGAGCCGCGAGCTCAGGCGGAGTACTACTCAACCATCATCACTAAGCCAGC 120
Db 61 AAGCGCATGAGCCGCGAGCTCAGGCGGAGTACTACTCAACCATCATCACTAAGCCAGC 120
Qy 121 CAGTGGGAGGGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGG 180
Db 121 CAGTGGGAGGGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGG 180
Qy 181 GCGAGGGTCCGCTGCTGCGACCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTG 240
Db 181 GCGAGGGTCCGCTGCTGCGACCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTG 240
Qy 241 TGGCGGAGGAGAGATCACTCCGCGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 300
Db 241 TGGCGGAGGAGAGATCACTCCGCGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 300
Qy 301 ATCCAGAGATCACTCCGCGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 360
Db 301 ATCCAGAGATCACTCCGCGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 360
Qy 361 TGCAGCTCAGCCAGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGG 420
Db 361 TGCAGCTCAGCCAGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGG 420
Qy 421 CCATTGGAAGAGCTCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTG 480
Db 421 CCATTGGAAGAGCTCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTG 480
Qy 481 GATTCCGCGCATCACTCATCTCTGCGCATGAGTGAAGGAGGAGGAGGAGGAGGAGGAGGAGG 540
Db 481 GATTCCGCGCATCACTCATCTCTGCGCATGAGTGAAGGAGGAGGAGGAGGAGGAGGAGGAGG 540
Qy 541 CGGCGGAGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGG 600
Db 541 CGGCGGAGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGG 600
Qy 601 ACCCGCGCATCTCCGCGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCG 660
Db 601 ACCCGCGCATCTCCGCGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCG 660
Qy 661 GCCCTTCAGAGTGGGGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGG 720
Db 661 GCCCTTCAGAGTGGGGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGG 720
Qy 721 GACCGCGCATCTCTCTTAAGAAATGACTTCAAGAGGAGGAGGAGGAGGAGGAGGAGGAGGAG 780
Db 721 GACCGCGCATCTCTCTTAAGAAATGACTTCAAGAGGAGGAGGAGGAGGAGGAGGAGGAGGAG 780

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Exhibit B

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Db      781 GGGCAGTGTGTGGAGGGGAGTGTTCAGAAAGAGGCTGTGTGACAGAGCCGCCCTGTG 840
Qy      841 TCCCCCAGAGTGTGTGGAGGAGAGCTGAGAGGCGGAAATGTTTCTAGTTAGGCCACGCTCC 900
Db      841 TCCCCCAGAGTGTGTGGAGGAGAGCTGAGAGGCGGAAATGTTTCTAGTTAGGCCACGCTCC 900
Qy      901 TCTGTTCAGTGTGCAAGAGTGAACACTCATGTGCGGAGCCATGGGCGCTCTGAGCAACTGTG 960
Db      901 TCTGTTCAGTGTGCAAGAGTGAACACTCATGTGCGGAGCCATGGGCGCTCTGAGCAACTGTG 960
Qy      961 CAGACCCCTTTCACCCCAATTAAACCCAGAACCACTTAAAAA 1014
Db      961 CAGACCCCTTTCACCCCAATTAAACCCAGAACCACTTAAAAA 1014

```

```

RESULT 3
US-10-616-410-1
; Sequence 1, Application US/10616410
; Publication No. US200503032A1
; GENERAL INFORMATION:
; APPLICANT: Hunter, Tony
; APPLICANT: Kun Ping, Lu
; TITLE OF INVENTION: NIMA INTERACTING PROTEINS
; FILE REFERENCE: 66671-043
; CURRENT APPLICATION NUMBER: US/10/616,410
; CURRENT FILING DATE: 2003-07-08
; PRIOR APPLICATION NUMBER: US 09/275,900
; PRIOR FILING DATE: 1999-03-24
; NUMBER OF SEQ ID NOS: 22
; SOFTWARE: FastSeq for Windows Version 4.0
; SEQ ID NO 1
; LENGTH: 1014
; TYPE: DNA
; ORGANISM: Homo sapiens
; FEATURE:
; NAME/KEY: CDS
; LOCATION: (25)...(513)
US-10-616-410-1

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Query Match      100.0%; Score 1014; DB 19; Length 1014;
Best Local Similarity 100.0%; Pred. No. 1.6e-274;
Matches 1014; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy      1 TGTGTGCGCAGACCTGTGAGGAGAGATGCGGAGAGGAGAGAGTCCCGCGCGCTGTGAG 60
Db      1 TGTGTGCGCAGACCTGTGAGGAGAGATGCGGAGAGGAGAGAGTCCCGCGCGCTGTGAG 60
Qy      61 AAGCGCATGAGCGGCGAGCTCAGGCGGAGTGTACTTCAACCAATCACTTAAGCGCAGC 120
Db      61 AAGCGCATGAGCGGCGAGCTCAGGCGGAGTGTACTTCAACCAATCACTTAAGCGCAGC 120
Qy      121 CAGTGTGAGAGGCGCGCAGCGGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 180
Db      121 CAGTGTGAGAGGCGCGCAGCGGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 180
Qy      181 GCGAGGGGTGCGTGTGTGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 240
Db      181 GCGAGGGGTGCGTGTGTGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 240
Qy      241 TGGCGGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 300
Db      241 TGGCGGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 300
Qy      301 ATCCAGAGAGATCAAGTGTGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 360
Db      301 ATCCAGAGAGATCAAGTGTGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 360
Qy      361 TGCAGCTCAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 420
Db      361 TGCAGCTCAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 420
Qy      421 CCAATTGAAGAGCGCTGTGTGTGCTGTGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 480
Db      421 CCAATTGAAGAGCGCTGTGTGTGCTGTGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 480

```

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Db      421 CCAATTGAAGAGCGCTGTGTGTGCTGTGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 480
Qy      481 GATTTCGGGATTCATCATCTCTCCGACCTGAGTGAAGGTGGAGAGAGAGAGAGAGAGAG 540
Db      481 GATTTCGGGATTCATCATCTCTCCGACCTGAGTGAAGGTGGAGAGAGAGAGAGAGAGAG 540
Qy      541 CGGGGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 600
Db      541 CGGGGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 600
Qy      601 ACCCCCACTCTCTGCGACCGGTCAAGATTAATTAATTCACCAATGAGCTGGAGAGAG 660
Db      601 ACCCCCACTCTCTGCGACCGGTCAAGATTAATTAATTCACCAATGAGCTGGAGAGAG 660
Qy      661 GCCCTTCAGATTTGGAGGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 720
Db      661 GCCCTTCAGATTTGGAGGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 720
Qy      721 GACCGGCAAGTTCTCCCTTAAGAGATTAATTAATTAATTAATTAATTAATTAATTAAT 780
Db      721 GACCGGCAAGTTCTCCCTTAAGAGATTAATTAATTAATTAATTAATTAATTAATTAAT 780
Qy      781 GGGCAGTGTGTGGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 840
Db      781 GGGCAGTGTGTGGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 840
Qy      841 TCCCCCAGAGTGTGTGGAGGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 900
Db      841 TCCCCCAGAGTGTGTGGAGGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 900
Qy      901 TCTGTTCAGTGTGCAAGAGTGAACACTCATGTGCGGAGCCATGGGCGCTCTGAGCAACTGTG 960
Db      901 TCTGTTCAGTGTGCAAGAGTGAACACTCATGTGCGGAGCCATGGGCGCTCTGAGCAACTGTG 960
Qy      961 CAGACCCCTTTCACCCCAATTAAACCCAGAACCACTTAAAAA 1014
Db      961 CAGACCCCTTTCACCCCAATTAAACCCAGAACCACTTAAAAA 1014

```

```

RESULT 4
US-10-648-631-1
; Sequence 1, Application US/10648631
; Publication No. US20050049404A1
; GENERAL INFORMATION:
; APPLICANT: Hunter, Tony
; APPLICANT: Kun Ping, Lu
; TITLE OF INVENTION: NIMA INTERACTING PROTEINS
; FILE REFERENCE: 66671-044
; CURRENT APPLICATION NUMBER: US/10/648,631
; CURRENT FILING DATE: 2003-08-25
; PRIOR APPLICATION NUMBER: US 10/616,410
; PRIOR FILING DATE: 2003-07-08
; NUMBER OF SEQ ID NOS: 22
; SOFTWARE: FastSeq for Windows Version 4.0
; SEQ ID NO 1
; LENGTH: 1014
; TYPE: DNA
; ORGANISM: Homo sapiens
; FEATURE:
; NAME/KEY: CDS
; LOCATION: (25)...(513)
US-10-648-631-1

Query Match      100.0%; Score 1014; DB 19; Length 1014;
Best Local Similarity 100.0%; Pred. No. 1.6e-274;
Matches 1014; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy      1 TGTGTGCGCAGACCTGTGAGGAGAGATGCGGAGAGGAGAGAGTCCCGCGCGCTGTGAG 60
Db      1 TGTGTGCGCAGACCTGTGAGGAGAGATGCGGAGAGGAGAGAGTCCCGCGCGCTGTGAG 60
Qy      61 AAGCGCATGAGCGGCGAGCTCAGGCGGAGTGTACTTCAACCAATCACTTAAGCGCAGC 120
Db      61 AAGCGCATGAGCGGCGAGCTCAGGCGGAGTGTACTTCAACCAATCACTTAAGCGCAGC 120

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Nucleic Acids, Linkers and Primers

Random Primer

This primer is used for radiolabeling any probe DNA to a high specific activity (1). The method, "oligolabeling" (1), has been optimized to allow greater control over the size of hybridization probes (2). Oligolabeling eliminates two sources of nuclease activity (DNAse I and 5'-3' exonuclease) that are associated with nick translation (3).

- Reference: 1. Feinberg, A.P. and Vogelstein, B. (1983) *Analytical Biochem.* 132, 6-13.
2. Fisk, F.Z. and Hodgson, C.P. (1987) *Nucleic Acids Res.* 15, 6295.
3. Maniatis, T., Jeffrey, T.A. and Kleid, D.G. (1975) *Proc. Nat. Sci. USA* 72, 1184-1185.

#1230	Random Primer 5'd(NNNNNN)3'	1.0 A ₂₆₀ unit	\$72
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Transcription
Promotor Primers

Three primers are available for sequencing plasmids containing T7, T3, or SP6 RNA polymerase promotor sequences. The T7 primer is complementary to conserved sequence in all of the class III promoters for T7 RNA polymerase (1). The SP6 primer can be used to sequence insertions in the polylinker regions of the pSP64 and pSP65 cloning vectors developed by Melton et al. (2). The T3 primer is complementary to the consensus sequence of the eleven class III promotor sequences for T3 RNA polymerase (3). Note: Primers can not be used for certain plasmids that contain truncated (but still fully functional) promoters.

All primers sequence in the direction of transcription and are supplied with a protocol using a modification of sequencing procedure for double-stranded DNA (4,5,6). With this protocol, sequencing information in excess of 350 base pairs can be obtained.

1.0 A₂₆₀ unit is approximately 40 µg.

- References: 1. Studier, W.F. and Dunn, J.J. (1983) *J. of Mol. Biol.* 166, 477-535.
2. Melton, D.A. et al. (1984) *Nucleic Acids Res.* 12, 7035-7056.
3. McAllister, W.T. et al. (1985) *Nucleic Acids Res.* 13, 6753-6766.
4. Chen, E.Y. and Seeburg, P.H. (1985) *DNA* 4, 165.
5. Hattlinger, M., Kempe, T. and Tijan, R. (1985) *Nucleic Acids Res.* 13, 1015-1025.
6. Gravel, R.A., Korneluk, R.G. and Qian, F. (1985) *Gene* 40, 317-323.

		0.1 A ₂₆₀ unit	1.0 A ₂₆₀ unit
#1226	SP6 Promotor Primer 24 MER 5'd(CATACGATTAGGTGACACTATAG)3'	\$75	\$288
#1227	T7 Promotor Primer 23 MER 5'd(TAATACGACTCACTATAGGGAGA)3'	\$75	\$288
#1228	T3 Promotor Primer 20 MER 5'd(ATTAAACCTCACTAAAGGGA)3'	\$75	

M13
Hybridization
Probe Primer

The M13 Hybridization Probe Primer can be used to generate a radioactive hybridization probe for a region of DNA or RNA which is complementary to a DNA fragment that has been cloned into any of the M13 λ phages (1). This primer does not prime through the cloned fragments. The 5' end of the primer anneals 46 nucleotides 5' to the cloning sites of the M13 λ phages. Synthesis is directed away from the cloning sites, making a complementary copy of the M13 vector DNA. Synthesis stops before the cloning sites are reached, leaving the inserted DNA single-stranded. Because of the single-stranded nature of the hybridizing DNA and the high specific activity achievable with *in vitro* DNA synthesis using radioactively labeled deoxynucleoside triphosphates, a very sensitive M13 hybridization probe is generated.

Reference: 1. Hu, N. and Messing, J. (1982) *Gene* 17, 271-277.

#1202	M13 Hybridization Probe Primer 16 MER 5'd(CACAATCCACACAAC)3'	0.1 A ₂₆₀ unit	\$75
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malE Primer

The *malE* Primer enables sequence to be derived from inserts cloned into plasmids pMAL-c and pMAL-p and is used in conjunction with the Protein Fusion and Purification System, see page 116.

#1237	<i>malE</i> Primer 5'd(GGTCGTCAGACTGTCGATGAAGCC)3'	0.1 A ₂₆₀ unit	\$75
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